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SUMMARY

A surveillance inspection of this US Corporate Headquarters was conducted pursuant to Memorandum dated 8/27/2010 from the Risk Management and Strategic Problem Solving Team (HFD-330), Office of Compliance, CDER under FACTS Assignment ID 1139556, Operation ID 4601042. CPGM 7353.001, Post-marketing Surveillance and Epidemiology: Human Drugs, afforded inspectional guidance.

The previous inspection conduct in September of 2007 determined that this facility does not manufacture or test drug products for commercial distribution. The inspection was classified NAI.

The current inspection was a Post-marketing Adverse Drug Experience (PADE) inspection. The inspection revealed that for NDA ((b) (4) Aleve Gelcaps and NDA #21-472, Midol Liquid Gels, for 129 case versions received that were both serious and unexpected, 104 case versions were submitted past five calendar days to the applicant. A FDA-483 issued to Wes E. Cetnarowski, SVP Global Research and Development on September 10, 2010. Dr. Cetnarowski promised corrective actions in writing to the district within 15 calendar days.

ADMINISTRATIVE DATA

Inspected firm:	Bayer Healthcare, LLC
Location:	36 Columbia Rd Morristown, NJ 07960-4526
Phone:	973-254-5000
FAX:	(973)254-4875
Mailing address:	P.O. Box 1910 Morristown, NJ 07962-1910
Dates of inspection:	9/7/2010, 9/8/2010, 9/9/2010, 9/10/2010
Days in the facility:	4
Participants:	Addam S. Reynolds, Investigator

On September 7, 2010, I, Investigator Addam S. Reynolds, presented my credentials and issued a FDA-482, Notice of Inspection, to Ajay Chawla, Head Technical Regulatory Affairs. Mr. Chawla indicated that he was authorized to accept the Notice.

During the inspection, Mr. Chawla was the primary contact at the firm. He answered questions, provided documents, made employees available when needed. Other Bayer Healthcare LLC employees that participated in the inspection include:

Stephen Klincewicz, Head of Global Drug Safety
Ravi Patel, Deputy Director Affiliates, Alliance, and Compliance Monitor
(b) (4), Consultant (Bayer Schering Pharma AG)

The before mentioned Bayer Consumer Care employees report ultimately report to Gary Balkema, Head of Consumer Care. A copy of the firm's organizational chart is included as **Exhibit #1**.

A close-out meeting was held with the firm on September 10, 2010. The attendees of the meeting were: Mr. Chawla, Dr. Klincewicz, and Wes E. Cetnarowski, SVP Global Research and Development. A FDA-483, Inspectional Observations, was issued to Dr. Cetnarowski. Dr. Cetnarowski promised corrective actions in writing to the district.

HISTORY

The Consumer Care Division of Bayer Healthcare LLC is headquartered at 36 Columbia Road, Morristown, NJ 07962. The Global Headquarters of the firm's parent company, Bayer Healthcare,

AG is located in Germany. The firm's most responsible person is Dr. Joerg Reinhardt for Bayer Healthcare LLC; the Head of the Consumer Care Division is Gary Balkema. Dr. Balkema maintains an office at this site.

The Consumer Care Division markets over-the-counter (OTC) drug products in the United States that are covered under approved applications and/or OTC monographs. In addition the Consumer Care Division also markets dietary supplements

This location employs (b) (4) employees; the pharmacovigilance department employs (b) (4) individuals. Hours of operation are from (b) (4) . For fiscal year 2009, the firm reportied annual earnings of (b) (4) Euros.

All FDA correspondence should be addressed to:

Wes E. Cetnarowski, SVP Global Research and Development
Bayer Healthcare LLC
P.O. Box 1910
Morristown, NJ 07962-1910

INTERSTATE COMMERCE/JURISDICTION

The firm is the Global Headquarters for Bayer Consumer Care Products. Attached is the firm's current list of products being marketed in the United States (**Exhibit #2**). This site acts as the firm's center for regulatory affairs, pharmacovigilance, and research and development. Commercial products are not manufactured or distributed at this site.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Stephen Klincewicz, Head of Global Drug Safety: Dr. Klincewicz is responsible for the oversight of the Consumer Care Division's Global Drug Safety Department. He is responsible for case processing, risk management, pharmacovigilance, and associated quality, training, and compliance activities. Dr. Klincewicz reports to Wes Cetnarowski, SVP Head Global Research and Development.

Ravi Patel, Deputy Director Affiliates, Alliance, and Compliance Monitor: Mr. Patel is responsible for the oversight of ensuring compliance with applicable regulations within the Bayer organization, including affiliates, and license agreements. Mr. Patel provided information pertaining to reporting requirements for adverse events where Bayer Healthcare is not the applicant holder.

(b) (4) *, Consultant Bayer Healthcare AG:* The primary scope of his consultancy is limited to Global single case process within Bayer Schering Pharma as well as his expertise regarding the (b) (4) Database and all related tools used for the global processing of case information.

Ajaw Chawla, Head Technical Regulatory Affairs: Mr. Chawla is responsible for overseeing the Regulatory Affairs group. He is also responsible with ensuring the timely submission and maintenance of regulatory filings. Mr. Chawla was the main point of contact during the inspection.

FIRM'S TRAINING PROGRAM

I reviewed the firm's training program. Currently at this facility three individuals currently have reporting responsibility during the transition of pharmacovigilance responsibility from Bayer Schering Pharma. I reviewed training records related to these individuals; I noted that required training has been completed or is in the processing of being completed according to the established schedule; no deficiencies were noted.

PHARMACOVIGILANCE OPERATIONS

At the time of this inspection, all pharmacovigilance related activities for the Consumer Care Division (BCC) was contracted to Bayer Schering Pharma's (BSP) Global PV and Bayer Healthcare Pharmaceutical Division. Specific services contracted to these organizations include: maintenance of the validated computer database, single case management and reporting, signal detection, periodic reporting, and all other consultations.

As of September 2010 BSP provides case processing and aggregate reporting activities. BCC is in the process of (b) (4)
(b) (4) Currently, three employees of BCC process cases for reporting to the Agency. These individuals follow BSP SOPs and training procedures. By the end of 2010 BCC will perform local triage and partial case entry, while BSP will continue to perform full case reporting during the transition. BCC will take responsibility for generating PADERs and Annual Reports for consumer products. BCC will train on BSP SOPs for most processes and will develop their own SOPs for consumer specific procedures.

Aggregate Reporting

I requested a line listing for all application products, late annual reports and periodic safety reports. In the past two years there has only been only late periodic safety report, for Bayer Migraine NDA#21-317. The due date for submission was April 1, 2010; the report was submitted May 5,

2010, representing 34 days late. This product is not currently marketed in the United States. Please refer to the *General Discussion with Management* section of this EIR for further details.

15-day Alert Reporting

I requested the compliance statistics for 15-day alert reporting for all products. The compliance statistics Compliance statistics cover the reporting period of 9/2008 thru 8/2010. Out of 3,231 serious, unexpected reports received, 230 cases were reported past the 15 day timeframe. Please refer to the *General Discussion with Management* section of this EIR for further details.

5-day Reporting to Application Holders

BCC markets four products where Bayer Healthcare is not the applicant holder; I requested compliance statistics for each product. Attached as **Exhibit #3** are the compliance statistics and individual line listing of cases for Perrigo ANDA 76-518, Aleve D Sinus & Cold. Attached as **Exhibit #4** are the compliance statistics and individual line listing of cases for (b) (4), Midol Maximum Strength Cramp and Body Ache. Attached as **Exhibit #5** are meeting minutes between Bayer and (b) (4) to discuss changes to their PV agreement where Bayer would. No significant deficiencies were found with reporting for these products.

For (b) (4) and 21-472, Aleve Gelcaps and Midol Liquid Gels, respectively, I requested compliance statistics and a line listing for late report. Please refer to the *Objectionable Conditions and Management's Response* section of this EIR for further details.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE

Observations listed on form FDA 483

OBSERVATION 1

You, as a non-applicant, elected to submit to the applicant (rather than to FDA) all reports of adverse drug experiences that were both serious and unexpected. However, you did not submit each report to the applicant within five calendar days of your receipt of the information.

Specifically, for Aleve Gelcaps (NDA #(b) (4) and Midol Liquid Gels (NDA #21-472) out of 129 case versions submitted to the applicant, 104 case versions were submitted past five calendar days. For example:

Event ID	Version	Date Received	Date Submitted
200913193BCC	1.0.25	8/19/2009	9/15/2009

200914757BCC	1.0.8	9/17/2009	10/14/2009
200915078BCC	1.0.7	10/1/2009	10/9/2009

Reference: 21 CFR 314.80(c)(1)(iii)

Supporting Evidence and Relevance:

I requested compliance statistics for reporting adverse events to (b) (4) for Aleve Gelcaps (NDA #(b) (4) and Midol Liquid Gels (NDA #21-472) (**Exhibit #6**). I requested a line listing of those cases where the firm identified a serious, unexpected case where product manufactured by (b) (4) was included (**Exhibit #7**). 260 case versions were submitted to (b) (4) as per the firm's PV agreement. Of these cases 260 cases, 129 were considered to be serious, unlisted and would have resulted in a 15-day alert report if Bayer had direct reporting responsibly. Out of 129 cases reportable, 104 were submitted to (b) (4) past the 5 calendar days.

I selected three cases to review in order to validate the accuracy and reliability of the line listing and statistics the firm provided. Individual Case Safety Reports (ICSRs) reviewed include:

Event ID	Version	Date Received	Date Submitted	Exhibit #
200913193BCC	1.0.25	8/19/2009	9/15/2009	**#8**
200914757BCC	1.0.8	9/17/2009	10/14/2009	**#9**
200915078BCC	1.0.7	10/1/2009	10/9/2009	**#10**

Review of the ICSRs revealed no further deficiencies.

Discussion with Management:

During the inspection and at the close-out meeting I discussed with the firm's management that for those ICSRs that are both serious and unexpected the firm must report such information to the applicant holder within 5 calendar days. I further stated that the Agency's expectation is that if the firm is unable to report within 5 days to the applicant holder that the firm should submit a 15-day alert report directly to the Agency. The firm's management understood my concern and agreed. The firm committed to sending a written response to the district within 15 calendar days.

REFUSALS

No refusals were encountered during the current inspection.

GENERAL DISCUSSION WITH MANAGEMENT

A close-out meeting was held with the firm on September 10, 2010. The attendees of the meeting were: Mr. Chawla, Dr. Klincewicz, and Wes E. Cetnarowski, SVP Global Research and Development. A FDA-483, Inspectional Observations, was issued to Dr. Cetnarowski. Dr. Cetnarowski promised corrective actions in writing to the district.

The following issues were discussed with the firm, but not documented on an FDA-483, Inspectional Observations:

Late Aggregate Reports

I requested to review the firm's compliance statistics for late annual reports and periodic safety reports. For NDA 21-317, Bayer Migraine the firm submitted the periodic safety report (PSR) 34 days late (**Exhibit #11**). The PSR was submitted on May 5, 2010 and was due on April 1, 2010. I noted that at the current time this product is not marketed in the United States.

During the closeout meeting I reminded the firm's officials that PSRs need to be submitted to the Agency within the required timeframe. I further stated that this inspectional finding was not documented on an FDA-483, Inspectional Observations as the product is not currently marketed in the United States. I stated that had this product been marketed in the United States this late submission would have been documented on an FDA-483. The firm's management understood my concern and agreed.

Late 15-day Alert Reports

I requested to review the compliance statistics for 15-day alert reporting (**Exhibit #12).** Over the two year reporting period of 9/2008-8/2010 I noted that out of 3,231 cases that were both serious and unexpected, 230 cases were submitted based the 15-day timeframe.

I noted that in January 2010, 40% of cases reported in that timeframe were submitted late to the Agency. The firm explained that during this period a publication, the Annual Poison Report, is published where a large number of ICSRs are generated. I reviewed the firm's related CAPA; corrective actions appeared adequate.

I also noted that in May 2010, 25.7% of cases reported in that month were submitted late to the Agency. The firm explained that during this period the BSP database, (b) (4) received a medical terms update. This caused a significant increase of ICSRs generated. I reviewed the firm's related CAPA; corrective actions appeared adequate.

During the inspection and during the closeout meeting I stated that the firm must report ICSRs that are both serious and unexpected to the Agency within the 15 day timeframe. I also stated that this inspectional finding was not documented on an FDA-483, Inspectional Observations, as an inspection at BSP Global PV in Montville, NJ documented late 15-day alert reports, which included the consumer care products. I stated during the close-out meeting that the firm still has the responsibility to ensure that their contractors are meeting regulatory requirements. The firm's management agreed with my concern.

EXHIBITS COLLECTED

1.) Organizational Chart, 4 pages
2.) Marketed Products List, 5 pages
3.) ANDA 76-518 Compliance Data, 2 pages
4.) ANDA 70-481 Compliance Data, 2 pages
5.) Meeting Minutes, Bayer (b) (4) 1 page
6.) (b) (4) Reporting Compliance Statistics, 1 page
7.) (b) (4) Reporting Line Listing, 4 pages
8.) ICSR 200913193BCC, 13 pages
9.) ICSR 200914757BCC, 5 pages
10.) ICSR 200915078BCC, 4 pages
11.) Late Annual/Periodic Submissions, 1 page
12.) Compliance Statistics for 15-day Alert Reports, 1 page

ATTACHMENTS

1. FDA-482, Notice of Inspection, dated 9/7/2010, 1 page
2. FDA-483, Inspectional Observations, dated 9/10/2010, 1 page
3. Memorandum dated 8/27/2010 from the Risk Management and Strategic Problem Solving Team (HFD-330), 3 pages

Addam S. Reynolds, Investigator